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Prescription Drug Monitoring Program Data Tracking of Opioid Addiction Treatment Outcomes in Integrated Dual Diagnosis Care Involving Injectable Naltrexone

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Background and Objectives: Fourfold increases in opioid prescribing and dispensations over 2 decades in the U.S. has paralleled increases in opioid addictions and overdoses, requiring new preventative, diagnostic, and treatment strategies. This study examines Prescription Drug Monitoring Program (PDMP) tracking as a novel measure of opioid addiction treatment outcomes in a university-affiliated integrated mental health-addiction treatment clinic.
Methods: Repeated measure parametrics examined PDMP and urine drug screening (UDS) data before and after first injection for all patients ($N = 68$) who received at least one long-acting naltrexone injection (380 mg/IM) according to diagnostic groupings of having either (i) alcohol (control); (ii) opioid; or (iii) combined alcohol and opioid use disorders.
Results: There were no group differences post-injection in treatment days, injections delivered, or treatment service encounters. UDS and PDMP measures of opioid exposures were greater in opioid compared to alcohol-only patients. Post-first injection, UDS's positive for opioids declined ($p < .05$) along with PDMP measures of opioid prescriptions ($p < .001$), doses ($p < .01$), types ($p < .001$), numbers of dispensing prescribers ($p < .001$) and pharmacies ($p < .001$). Opioid patients without alcohol disorders showed the best outcomes with 50% to 80% reductions in PDMP-measures of opioids, down to levels of alcohol-only patients.
Conclusions: This study shows PDMP utility for measuring opioid addiction treatment outcomes, supporting the routine use of PDMPs in clinical and research settings.
Scientific Significance: These findings demonstrate that opioid addiction in patients with complex addictions and mental illnesses comorbidities can show effective treatment responses as measured by PDMP tracking of decreases in opioid prescriptions to those patients. (Am J Addict 2016;25:557–564)

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INTRODUCTION

From 1999 to 2008, the U.S. has experienced a fourfold increase in opioids prescribed and dispensed for pain indications, with proportional increases in addiction treatment episodes and prescription drug overdose deaths.[1] By 2008, prescription drug overdoses were occurring at rates nearly twofold higher than overdoses caused by heroin and all other illicit drugs combined, surpassing U.S. death rates caused by car accidents, suicides, or homicides.[1] In 2010, annual health care expenditures nationwide, just for treating overdoses, but not addiction, reached $2.3 billion, nearly double the annual extramural budget of the National Institutes on Drug Abuse.[2]

This public health crisis, listed as an epidemic by the CDC,[3] has been linked to medical-cultural shifts happening over 2 decades that have promoted opioid prescribing from primary care doctors and specialists, at increased doses, in poly opioid combinations, for greater durations, and in more clinical contexts.[4–6] Although the health, economic, and social consequences of the prescription opioid epidemic are broad,[7,8] people with mental illness and non-opioid addictions show disproportionate risk of suffering serious complications of increased access to prescription opioids.[9–12] Pre-existing mental illness is major risk factor for acquisition of opioid use disorders, and non-medical opioid use that escalates to addiction is a risk factor for onset of mental illness.[13] Whether produced by "Adverse Selection" where doctors are more likely to prescribe high risk opioid regimens to high risk (eg, mentally ill/addicted) patients,[14,15] or biological vulnerability to addictions in mentally ill brains,[16,17] strong linkages between mental illness and opioid addictions indicate the need to recognize and treat prescription opioid addictions in behavioral health settings.

Prescription Drug Monitoring Programs (PDMPs) are state-supported databases that allow instant access to outpatient controlled drug prescriptions and dispensation records. PDMPs are important new tools for preventing dangerous addictive drug prescribing, and for diagnosing and treating opioid addictions.[11,18] Our prior study using Indiana's PDMP (INSPECT: INdiana Scheduled Prescription Electronic Collection and Tracking) demonstrated PDMP utility as a diagnostic tool and for identifying detrimental opioid prescribing to mentally ill/addicted patients.[11] The present study extends these findings, by showing that PDMP inquiry can be utilized as a repeated measure for treatment outcome monitoring. We examined a population of patients selected by the sole criterion that they had received one or more doses of long-acting injectable naltrexone (INTX) (trade name Vivitrol; 380 mg IM) within a 12-month study window, for FDA-approved indications of opioid and/or alcohol use disorder.[19] The study cohort of 68 patients was thus naturalistically composed of three subgroups determined by their INTX diagnostic indication of having either (i) alcohol; (ii) opioid, or (iii) combined alcohol and opioid use disorders. This design, in which alcohol patients without opioid use disorders served as a control group, allowed us to examine the diagnostic specificity and utility of longitudinal PDMP data for opioid treatment outcome measurement, simultaneous with, and in comparison to urine drug screening, in a clinically realistic cohort of patients complicated by a diversity of comorbid addictions and mental illnesses.

METHODS

Setting, Study Population, and Design

The study took place in an integrated dual diagnosis outpatient clinic of Midtown-Eskenazi, the major community mental health center of downtown Indianapolis, IN, which hosts the addiction psychiatry fellowship training program of Indiana University Department of Psychiatry. It carries a census of 250–350 patients, referred from families, child protective services, probation courts, and health care facilities throughout Indianapolis. The clinic is staffed by a multidisciplinary team of nurses, masters-level therapists, case managers, board-certified addiction psychiatrists, addiction psychiatry fellows, and residents. It provides comprehensive-integrated dual diagnosis treatment to all patients without referring them out, regardless of what mental illness and addiction combination they may have; all of the patients included in this study were engaged, in an individualized way, in fully integrated dual diagnosis care involving both medication and psychotherapeutic treatments (including individual and group therapies) for both mental illness and addiction.

Data Collection

Medical record and PDMP data were collected for all patients that had been diagnosed by the addiction psychiatrist (or fellows and residents under their supervision) using DSM-IV criteria, and treated for the indication(s) of alcohol and/or opioid use disorder with at least one injection of long-acting injectable naltrexone (INTX) (Vivitrol; 380 mg IM) between August 1, 2012 and August 1, 2013. Data tracking ended for all cases on September 1, 2013. No patients had previously received any prior INTX injections, and none had treatment histories at the VA. There were no exclusions based on any demographic or diagnostic comorbidity. The study was designed as a before and after comparison, anchored on the date of the first INTX injection, between three naturalistically formed INTX indication groups composed of patients with: (i) alcohol (ETOH); (ii) opioid (OP); or (iii) both opioid and alcohol use disorders (OP + ETOH). Following the template of our prior PDMP study,[11] we collected key demographic and physician-assessed diagnostic data (Axis I mental health and substance diagnoses, Axis II disorders), concurrent with the time of first INTX injection, which was generally one of the first appointments with the psychiatrist. Chart review also provided number of treatment service encounters (individual or group sessions, including therapist, nursing, and doctor's appointments), and total number of INTX injections. Key outcome data collected for time periods before and after first INTX injection (pre- vs. post-injection phases) included urine drug screening (Redwood Laboratories, Santa, Rosa, CA; testing for up to 10 different substances including morphine, codeine, hydrocodone, oxycodone, buprenorphine, methadone, amphetamine, cocaine, tetrahydrocannabinol (THC), and Ethylglucoronide (ETG), a direct metabolite of ETOH[20]), and PDMP data (INSPECT). INSPECT provided a record of controlled substance outpatient prescribing (types, quantities, dates of prescription and fills, prescribers and pharmacies) dispensed from all Indiana retail pharmacies (except not from Indiana's Veterans Administration pharmacies in Indiana, or methadone dispensed from methadone treatment programs for opioid use disorders, which at the time of this study, still had not become transparent to INSPECT).[11]

For all subjects, the pre-injection phase was defined as the span of 1 year prior to the date of first INTX injection. This phase mostly encompassed time when patients had not yet entered treatment in our clinic, as well as about 2 months from the time they had entered treatment (eg, undergoing detoxification and/or starting individual and group therapies) to when they were first evaluated by a psychiatrist, which was required for starting INTX. The post-injection phase spanned time from the first INTX injection to the closing date of the study. Unlike the 1-year pre-injection phase, the post-injection phase was of variable durations between subjects, averaging ~7 months when patients were engaged in care. This study was evaluated and approved by the IU School of Medicine Institutional Review Board.

Data Analysis

Analysis of the post-injection treatment parameters (days post injection, number of injections, service encounters) was conducted as simple One-way Analyses of Variance (ANOVAs), where the independent factor (INTX indication

group) had three levels (ETOH only; OP only; OP + ETOH). For analysis of PDMP and UDS data, we utilized a mixed model, Repeated Measures ANOVA; dependent measures were compared across the pre- versus post-injection phases according to the INTX indication group factor. Analysis of UDS data looked at percentages of UDS tests collected that were positive, since frequencies of UDS testing were variable between patients, and the pre-injection phase encompassed much time when patients were not in treatment. This analysis was conducted first, for all individual tests among all 10 substances tested (including 6 opioids and amphetamines, cocaine, THC and ETG); second, for ETG tests only; and third, for tests of the 6 opioids only (morphine, codeine, hydrocodone, oxycodone, buprenorphine, methadone). For PDMP data, raw numbers of opioid prescriptions and opioid pills dispensed were adjusted in the post-injection phase to rates/year, to account for differences in durations in the pre- versus post-injection phases across patients (eg, if the post-injection phase was 9 months in duration, the raw values were divided by .75 years). Consistent with our prior study[11] we did not translate the quantities of prescribed opioids to morphine equivalents. The raw data for opioid pills dispensed showed extreme right-skewing, so this data was further transformed to log base 2 (of opioid pills) for parametric testing. PDMP outcome measures that tended to be stable (ie, did not increase linearly with time, including # of different generic types of opioids prescribed, different prescribers, different pharmacies) were directly compared pre- and post-injection without adjustment. Significant interactions between the repeated measure and group were followed up as One-way, single-level repeated measure ANOVAs, to specify which group showed the most significant change from pre to post-injection phases. All data in tables and graphs are reported as means + SEMS with all significant ($p < .05$) results presented throughout along with key non-significant (NS) results.

RESULTS

Demographics and Diagnostic Spectrum

The study population ($N = 68$) was 59% female, about two thirds white, and two-thirds uninsured (ie, with no insurance, where Midtown-Eskenazi bore the cost of care) (Table 1). Over half the patients were between ages of 26 and 45 years. A large majority (91%) had some type of Axis 1 non-substance disorder, with unipolar depression diagnosed most often, 66% of cases. Axis II conditions were diagnosed in 37% of cases, with Personality Disorder NOS found most frequently (22%). All patients were diagnosed with a substance use disorder with 53% having ETOH but not opioid use disorder, 28% having opioid use disorder without ETOH use disorder, and 18% having both. Tobacco use disorder was the second most common addiction in the population, found in 59%, second only to ETOH use disorder (72%), and exceeding opioid (47%) and cannabis use disorders (35%). The population had a high degree of comorbidity (Table 2) with a majority of having 3 or more addictions, and 2 or more mental illnesses. Five or more DSM-IV diagnoses were found in 40% of the study population, while much smaller minorities had no diagnosable axis I or II mental illness (7%) or only addiction involving just one substance (21%).

TABLE 1. Demographics and clinical diagnoses of study population ($N = 68$)

Demographic	*n* (%)
Age	
≤25 y	5 (7)
26–45 y	37 (54)
>45 y	26 (38)
Gender	
Female	40 (59)
Male	28 (41)
Ethnicity	
Black	23 (34)
White	42 (62)
Bi-racial	3 (4)
Insurance	
Medicaid/Medicare	25 (37)
Uninsured (Self pay/Hospital subsidy)	43 (63)
Diagnoses	
Axis 1 mental illness	
Any Axis 1 (non-substance use disorder)	62 (91)
Psychotic spectrum	4 (6)
Bipolar spectrum	11 (16)
Unipolar depression spectrum	45 (66)
Anxiety spectrum	22 (32)
PTSD	9 (13)
Axis 2 mental illness	
Any personality disorder	25 (37)
Borderline	9 (13)
Anti-social	1 (2)
Personality disorder NOS	15 (22)
Axis 1 substance use disorder	
Any substance use disorder	68 (100)
ETOH dependence	49 (72)
Opioid dependence	32 (47)
ETOH but not ppioid	36 (53)
Opioid but not ETOH	19 (28)
Both ETOH and ppioid	13 (19)
Benzodiazepine abuse/dependence	14 (21)
Cannabis abuse/dependence	24 (35)
Nicotine dependence	40 (59)
Stimulant (cocaine/amph) dependence	20 (29)

Treatment Groups

Among $n = 32$ patients with opioid use disorder, 17 had been using heroin and prescription opioids (10 in the opioid only group; 7 in opioid and ETOH group) while the remaining 15 had used prescription opioids only. Of these $n = 32$, 7 had also been prescribed buprenorphine at some point in the pre-

TABLE 2. Frequencies of diagnostic comorbidities (within $N = 68$)

Diagnostic class(s)	# Diagnoses per patient	*n* (%)
Mental illness[a]	0	5 (7)
	1	27 (40)
	2	21 (31)
	3	13 (19)
	4	2 (3)
Substance use disorders	0	0 (0)
	1	14 (21)
	2	16 (24)
	3	20 (29)
	4	15 (22)
	5	3 (4)
Mental illness + substance use D/O[b]	0	0 (0)
	1	1 (2)
	2	6 (9)
	3	17 (25)
	4	17 (25)
	5	10 (15)
	6	6 (9)
	7	9 (13)
	8	2 (3)

[a]Non-substance use disorder, inclusive of all combinations of Axis 1 and 2; [b]all comorbid combinations of Axis 1 (mental illness and substance use disorder) and Axis 2.

injection phase. This included 2 patients with both opioid and ETOH disorders that had been prescribed buprenorphine prior to entering our clinic, 1 patient with both diagnosis that had been prescribed buprenorphine in our clinic (prior to INTX), and 4 others that had opioid disorders only, who were initially prescribed buprenorphine, then converted to INTX in our clinic. Clinical parameters of the post-injection treatment phase, according to indication group are shown in Table 3. There were no differences between the groups in treatment days post-initial injection ($F[2,65] = .35$, NS), injections delivered per patient ($F[2,65] = .04$, NS), or mean number of days post-initial injection per injection (inter-injection interval) ($F[2,65] = .12$, NS). The number of treatment service encounters over the post-injection treatment phase (adjusted by duration of the post-injection phase) trended differently (but insignificantly $F(2, 65) = 1.9$, NS) according to group so that patients with both ETOH and opioid addiction used the most services (81.9 + 18.8/year) compared to 62.8 + 16.0/year for opioid only patients, and 46.5 + 7.2/year for ETOH only patients.

Urine Drug Screening Outcomes

The mean number UDS collected per patient (counted as sum of all collections including all 10 drug types) for each group during the pre- versus post-injection phases, are shown in Table 3. Although the total fraction of UDS tests that were positive (for any substance) trended downward for both groups with opioid disorders from the pre- to post-injection phases (analyzed for the $n = 43$ patients who had UDS tests in both the pre- and post-injection phases) (Table 3), these changes only approached significance (phase: $F[1,40] = 3.0$, $p = .09$, NS); group: $F[2,40] = 1.5$, NS; group x2009;× phase $F[2, 40] = 2.5$, $p = .09$, NS). Similarly, when focusing on ETG testing only (Fig. 1A; analyzed only for the $n = 21$ patients that had ETG tests collected in both the pre- and post-injection phases) the fraction of positive ETG tests did not decline significantly (phase: $F[1,19] = .34$, NS) and did not differ significantly according to group ([$F(1,19) = .28$, NS]) or as a phase × group interaction ($F[1,19] = .02$, NS) . In contrast, when focusing on opioid testing (Fig. 1B), analyzed for $n = 42$ patients that had opioid tests collected in both the pre- and post-injection phases, there was a significant overall decline in the fraction of positive opioid tests (phase: $F[1,39] = 5.7$, $p < .05$) on top of an overall group difference where, as expected, groups with opioid disorders had higher overall fractions of opioid tests positive compared to patients with ETOH only (group: $F[2,39] = 6.0$, $p < .01$). Changes in the percent of positive opioid tests also varied by indication group attaining marginal significance (phase × group: $F[2,39] = 3.2$, $p = .05$).

Prescription Drug Monitoring Database Outcomes

PDMP measures of opioid prescribing covering all cases ($N = 68$), revealed significant changes from pre- to post-injection phases. Opioid prescriptions/year (Fig. 1C), while being higher in the opioid groups ($F[2,65] = 7.7$, $p = .001$), declined significantly after the initial injection depending on the diagnostic group (phase× group: $F[2,65] = 6.4$, $p < .01$). Post hoc analyses pinpointed significant declines in opioid prescriptions in only the opioid-only group (phase: $F^{1,18} = 9.7$, $p < .01$). Opioid pills dispensed/year (Fig. 1D) showed indication group differences (group: $F[2,65] = 5.2$, $p < .01$), with a significant decreases post-injection (phase: $F[1,65] = 10.3$, $p < .01$), that depended on the diagnostic group (phase × group: $F[2,65] = 6.1$, $p < .01$). Specifically, the decline in opioid pills was significant only in the opioid-only addiction group ($F[1,18] = 18.0$, $p < .001$). The number of different opioid types prescribed per patient (Fig. 1E), also differed by group ($F[2,65] = 5.7$, $p < .01$), with overall declines post-injection (phase: $F[1,65] = 14.7$, $p < .001$) that were group-related (phase × group: $F[2,65] = 4.8$, $p < .05$), where in post hoc testing significance was limited to the OP group ($F[1,18] = 16.7$, $p < .01$). The number of prescribers (Fig. 1F) was also different according to diagnostic group ($F[2,65] = 7.2$, $p < .01$) and declined significantly post-injection (phase: $F[1,65] = 19.8$, $p < .001$), with a significant phase × group interaction ($F[2,65] = 4.5$, $p < .05$). This interaction was further specified by post hoc analysis as being limited to the opioid-only patients ($F[1,18] = 29.3$, $p < .001$). A similar pattern was found in analysis of number of dispensing pharmacies (Fig. 1G: [group: ($F(2,65) = 6.2$, $p < .01$; phase: $F(1,65) = 28.6$, $p < .001$; phase × group: $F(2,65) = 5.6$, $p < .01$]), where both opioid-only patients

TABLE 3. INTX indication group characteristics

INTX dosing				Days post-injection per injection			
					Frequencies by range (days)		
Vivitrol indication	(*n*)	Days post-injection	Number of injections	Mean	<60	(60 < 120)	>120
ETOH	36	208 ± 11	2.8 ± .3	97 ± 11	12	17	7
OP	19	189 ± 23	2.7 ± .6	100 ± 15	6	7	6
BOTH	13	201 ± 23	2.7 ± .6	108 ± 22	6	2	5
					24	26	18

UDS testing		Total indiv. drug tests[a]			% Positive[b]	
Vivitrol indication	(*n*)	Pre	Post	(*n*)	Pre	Post
ETOH	36	13.4 ± 1.8	16.2 ± 2.8	22	6.5 ± 1.8	7.0 ± 1.9
OP	19	10.9 ± 2.0	12.7 ± 4.8	11	12.5 ± 3.4	11.7 ± 3.3
BOTH	13	13.2 ± 2.8	16.8 ± 4.3	10	16.3 ± 5.3	6.7 ± 3.5

[a]Total number of individual tests collected (spanning possible selections of morphine, codeine, oxycodone, hydrocodone, buprenorphine, methadone, cocaine, amphetamine, tetrahydrocannabinol, and ethylglucoronide); [b]percent positive tests for those subjects tested both before and after initial injection.

(phase: $F[1,18] = 14.0$, $p < .01$) and patients with opioid and alcohol disorders ($F[1,12] = 5.7$, $p < .05$) showed significant declines.

DISCUSSION

This study demonstrates PDMP utility in treatment outcome monitoring of patients with opioid addiction. We show that repeated PDMP data collections can be used not only to corroborate clinical diagnoses, but to gauge treatment response. If paired routinely with UDS testing in clinical practice, PDMP database inquiry may thus contribute to an increasingly informative tool kit of objective measures to compliment subjective (eg, craving) assessments, and other more general psychiatric, medical, and functional measures for guiding clinical decision-making and quantifying outcomes.

These findings build on prior research in the same clinic using PDMP for determining the exposure of a mentally ill/addicted population to hazardous controlled substance prescribing, and for use as a diagnostic tool.[11] This prior study found that a majority of patients in the census had been prescribed opioids over the year before addiction psychiatry evaluation, and that PDMP data collected independent from this evaluation was predictive of both opioid use disorders and personality disorder diagnoses. The design and data collection of the present study differed from the earlier 1 in 3 major ways: only patients receiving at least one INTX dose were included; PDMP data was routinely incorporated into the diagnostic workup of all patients; and, patients were grouped according to INTX indication for repeated PDMP data analyses. Nevertheless, both studies included patient populations that were similar demographically: 54% to 58% were between ages 26–45 years; 51% to 59% were female; 55% to 62% were white; 63% to 66% were uninsured. Frequencies of dual diagnosis comorbidities (having an Axis 1 mental illness with a concurrent substance disorder) were very high in both study populations (80% to 91%, respectively). The densities and patterns of dual diagnoses comorbidities, and racial/age demographics of patients with opioid use disorders found in the present study were also consistent with several urban clinical samples and large scale epidemiological surveys,[2,7,8,21–25] indicating the present findings are likely generalizable to many addiction treatment settings. Notably, the rates of comorbid alcohol use disorders among patients with opioid use disorders found in our sample (41%) were comparable to recent population data showing that 58% of patients with opioid use disorders have 12-month prevalence rates of alcohol abuse or dependence.[25]

The 3 diagnostic group/repeated measures design and cross-comparison with UDS testing provided helpful experimental controls and an informative and yet credible pattern of results. The 3 diagnostic groups did not differ by number of days followed after initial injection, number of injections given, inter-injection intervals, or number of clinical service encounters. However, as expected, UDS tests that were positive for opioids, and PDMP patterns of opioid prescribing, did vary significantly according to diagnostic group and were mutually consistent by showing higher opioids in the opioid-dependent groups compared to the ETOH-only group. In effect, the ETOH-only group served as a naturalistic control for examining the capacity of treatment to specifically reduce opioid exposure in patients with opioid addiction, and for demonstrating that PDMP monitoring is capable of capturing this outcome in a way that is diagnostically specific and expected. Accordingly, PDMP data revealed that INTX-associated treatment had its most profound effects in reducing opioid prescriptions, doses, opioid types, numbers

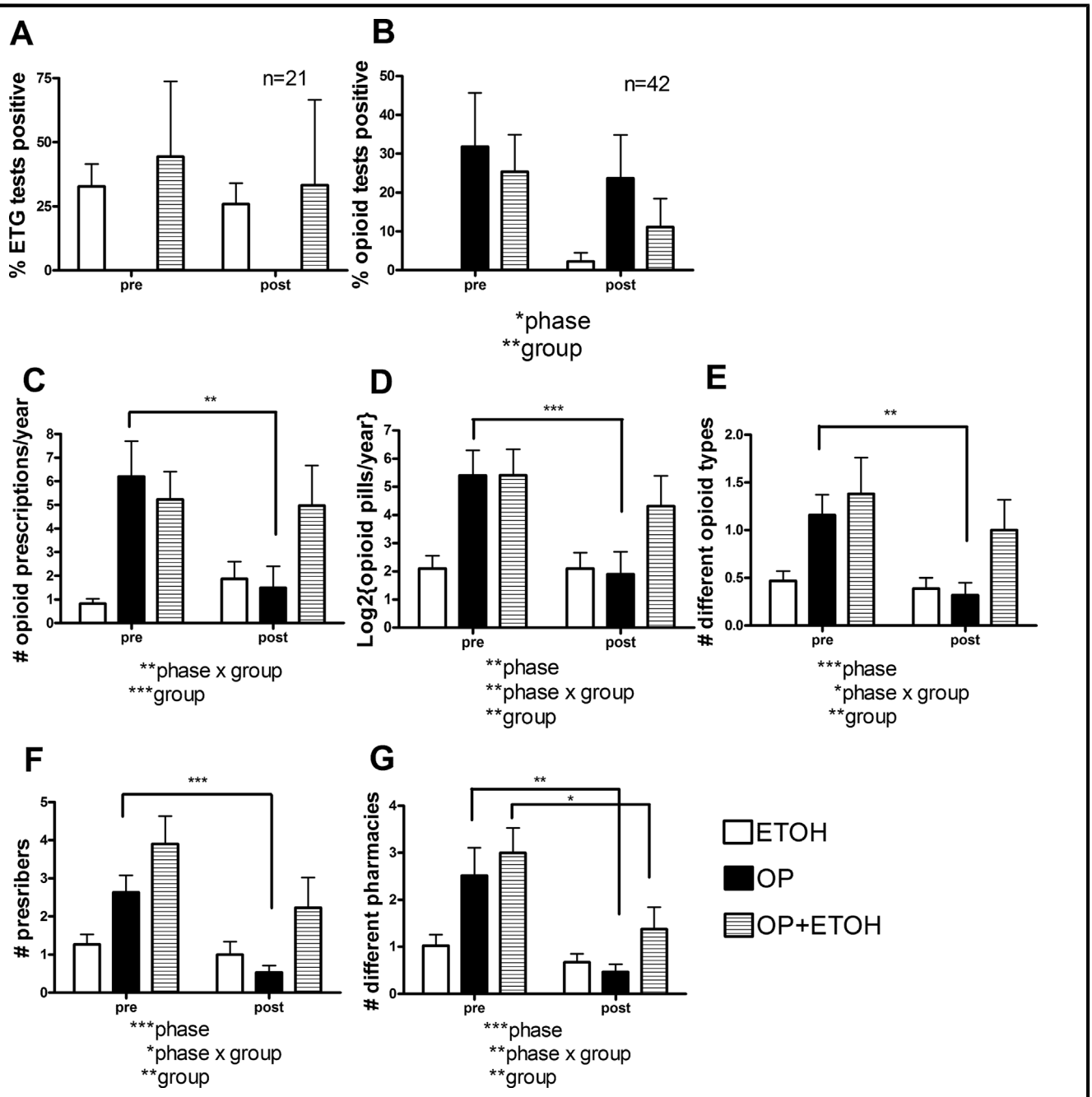

FIGURE 1. Urine drug test results (A and B), PDMP measures of opioid prescribing activity (C–E) and health care system involvement (F and G) pre versus post initial injection. (A) Percent of positive ETG tests trended downward non-significantly among the $n = 21$ subjects (ETOH, $n = 18$; OP + ETOH, $n = 3$) that had ETG testing both before and after initial INTX injection. (B) Percent of positive opioid tests differed by group and decreased post-injection among the $n = 42$ subjects (ETOH, $n = 22$; OP, $n = 11$; OP + ETOH, $n = 9$) that had opioid testing both before and after initial INTX injection (ETOH: Patients with alcohol without opioid use disorders; OP: patients with opioid but not alcohol use disorders; OP + ETOH patients with both alcohol and opioid use disorders). For all PDMP data (C–G) all $N = 68$ subjects are shown graphically and included in the statistical analysis. (C) The number of opioid prescriptions (adjusted to annual rates), differed between groups and dropped specifically in the OP group. (D) Annual adjusted numbers of opioid doses (normalized by Log base 2 transformation), differed by group, dropped overall, and in a significantly more robust way for the OP group. (E) Number of different types of opioids dispensed also differed by group, dropped overall, and in a more robust way for the OP group. (F) The number of prescribers dispensing controlled substances, differed by group, dropped overall, and in a significantly more robust way for the OP group. (G) The number of pharmacies dispensing controlled substances, differed by group, dropped overall, and in a significantly robust way for the OP and the OP + ETOH groups. Bars show means ± SEMS. Significant results from ANOVAs are noted where they occur ($^{*}p < .05$; $^{**}p < .01$; $^{***}p \leq .001$).

prescribers, and dispensing pharmacies in patients with opioid use disorders uncomplicated by alcohol disorders. These findings are in general agreement with studies indicating that the presence of multiple addictions renders patients more treatment refractory,[26,27] suggesting the need for more research into improving INTX efficacy in patients with comorbid opioid and alcohol disorders.

Both the strengths and limitations of the present study design should be considered in interpreting these results. The primary goal of the study was to demonstrate the utility of PDMP for monitoring treatment outcomes in the context of a treatment (INTX) that is already evidence-based and FDA approved. Accordingly, it was not designed as a clinical trial for INTX, and patients included in the study were being treated for a number of concurrent psychiatric and substances disorders using a range of different medications and psychotherapies. So, INTX treatment in this study deign served mainly as a discrete and certain temporal milestone to demark a "before" and "after" phase of treatment initiation, and was likely just one of a number of active therapeutic ingredients producing the clinical improvement documented by PDMP and UDS data. Future studies will need to discern how different therapies for opioid and other addictions and co-occurring mental illnesses produce efficacies as measured by PDMP data. A second major strength and weakness of the present study was its naturalistic design. Patients were not monetarily incentivized or diagnostically selected (other than having an indication for INTX injection) to participate in the research. Diagnostic workups and treatment strategies were highly individualized with quite variable, randomized use of UDS testing; greater standardization of UDS testing (ie, occurring in regular intervals, or with the same frequencies among all subjects), and uniformity of pre- and post-treatment intervals of PDMP data capture are needed in future studies. Greater experimental controls of treatment subgroup compositions in terms of comorbid diagnoses, type and timing of treatment choices or randomizations, and different mixes of insurance coverage, might produce more robust and/or nuanced effects in terms of PDMP-measured outcomes.

In summary, this study is the first to demonstrate the clinical utility of PDMP data collection as an objective measure of addiction treatment outcomes, and the first to verify the consistency of these data with UDS testing. These data lend support to calls for PDMP utilization to be routine or even mandatory in various practice contexts.[28] The study also illustrates what is likely to be a significant range of public health benefits of addiction prevention and treatment services that utilize PDMPs, for limiting unnecessary and potentially harmful healthcare practices associated with overprescribing of opioids.[29,30] In a population of mentally ill-addicted patients at risk for "Adverse Selection" phenomena,[14] PDMP monitoring showed that addiction and dual diagnosis treatment involving INTX objectively produced a significant decrease in exposure to prescribed opioids. This decrement was likely accompanied, to some extent that we did not measure, by reductions in costs associated with doctor's visits, medical diagnostic tests, pharmacy costs, and diversion of prescription drugs that often accompany iatrogenic opioid prescribing.[7,30,31] These findings thus suggest a remarkable, if indirect effect of addiction treatment, beyond individual patients, on the practices of outside physicians and health care systems that may inadvertently be contributing to addictions and overdose deaths. Along with educational and regulatory efforts designed to limit over-prescribing of opioids and other additive drugs, expanding psychiatric and dual diagnosis treatment services that incorporate PDMP utilization should be considered key strategies in reducing the prescription drug epidemic.

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Declaration of Interest

All authors have read the manuscript and approve of its submission to the American Journal on Addiction. RAC received a speaker's honorarium from Alkermes (American Psychiatric Association in Toronto, CA, May 2015), in no connection with this study and after its completion. There are no potential or actual conflicts of interest to report among the other authors.

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